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DISEASES OF THE NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

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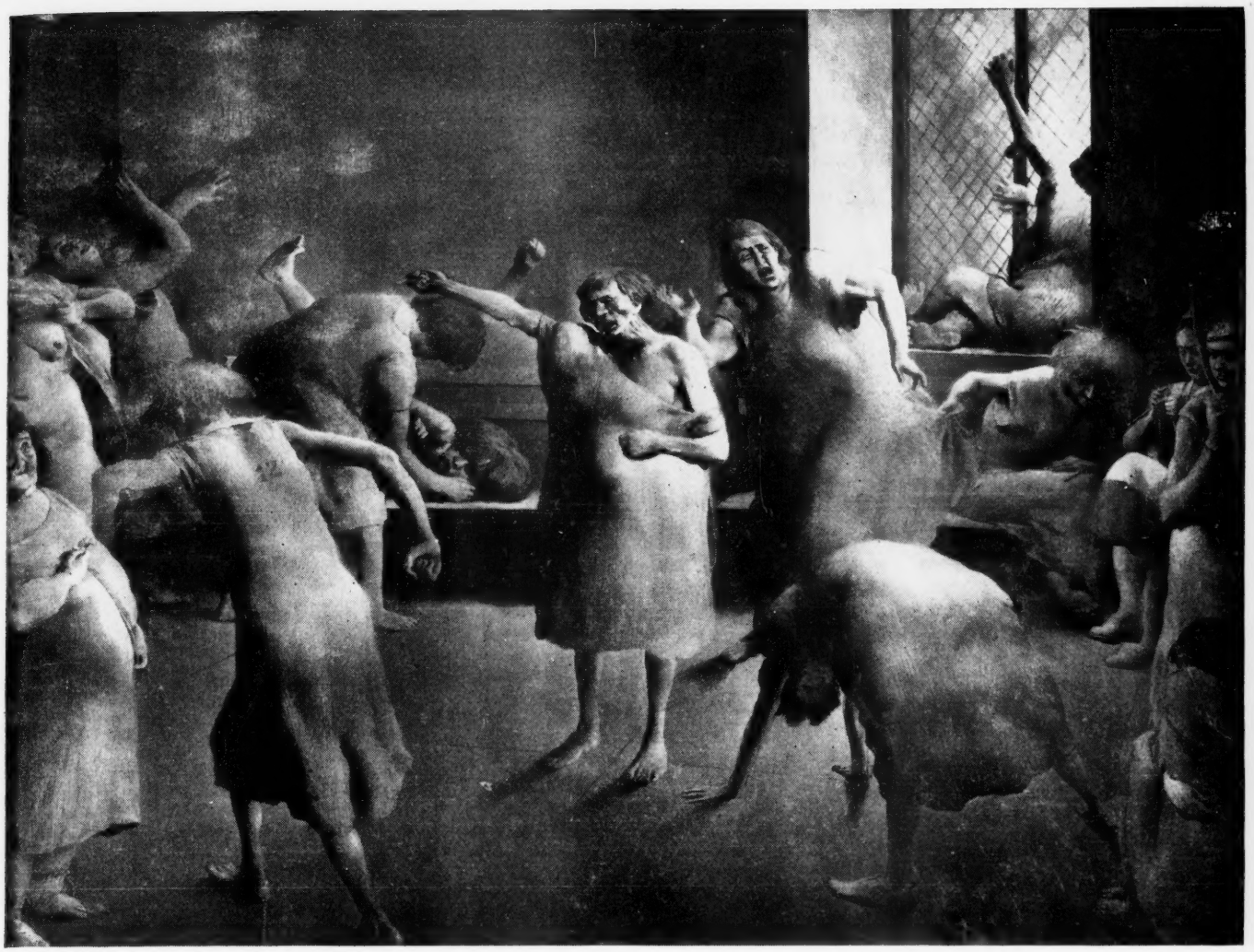

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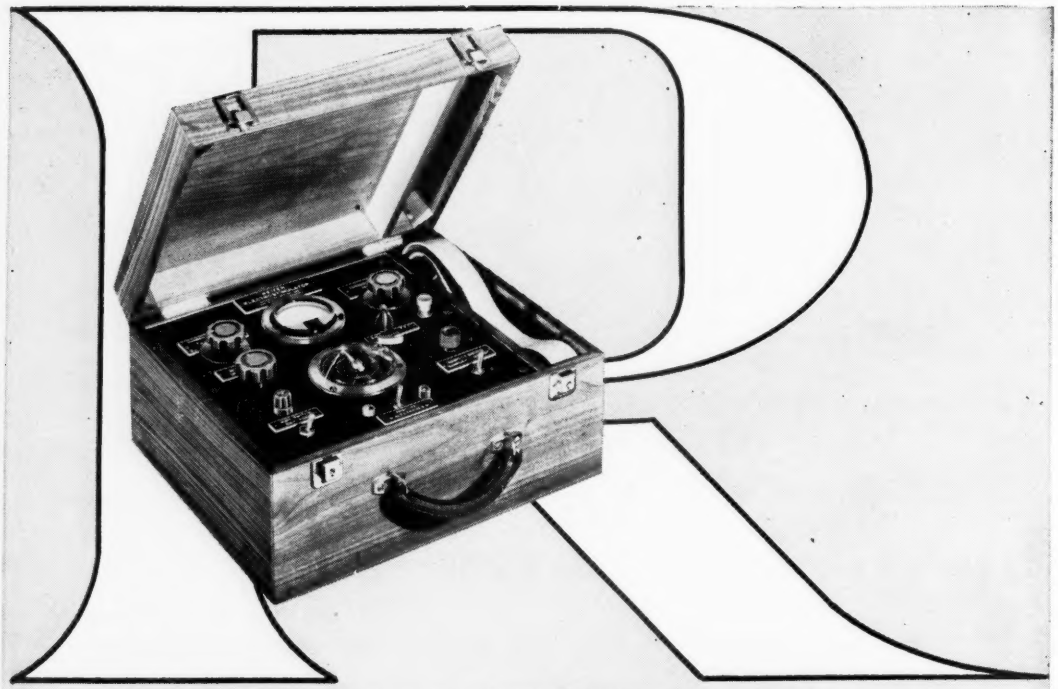

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DISEASES of the NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

Therapy of Acute Porphyria With Bal and Other Agents

(A Report of 19 Additional Cases)

HENRY A. PETERS, M.D.
Madison, Wisconsin

The ability of BAL (dimercaptopropanol) to reverse symptoms of acute porphyria was reported by Peters[1] and more recently by McCabe.[2] Striking effectiveness of the BAL treatment in a case of congenital porphyria (Günther's disease) with cutaneous lesions of hydroa-vacciniformis, epidermolysis bullosa-type, was recorded by Schrumpf.[3] Since the initial publication (1954), 21 additional cases manifesting an abnormal porphyrinuria have been found. Symptomatology justified the diagnosis of congenital porphyria in one case and the diagnosis of acute intermittent hepatic porphyria in 15 cases, of which 12 were observed during acute exacerbations of the neuropsychiatric disturbance; the remaining three could be classed as latent or subacute stages showing subtle symptomatology. Nine acute cases were given BAL treatment during major exacerbations with good response in six, questionable results in two and an unfavorable response in one. One case under BAL therapy required phenobarbital control of focal seizures but remained psychotic until the administration of Frenquel (4-piperidyl benzhydrol HCl) in dosage of 60 mg. orally daily for 4 days, following which she underwent a complete recovery. One case of acute porphyria with only abdominal colic was not benefiited by daily administration of 200 mg. intravenous Frenquel, but the symptoms were ameliorated by chelation with disodium calcium versenate (Ca EDTA) therapy. The residual abdominal pain in this patient continued despite added BAL therapy until procaine, 500 mg., was administered intravenously in 1,000 cc. normal saline solution daily for 2 days, following which she became asymptomatic. Recurrence of abdominal pain several weeks later was again treated with BAL and intravenous Procaine without complete relief. Dependence on Demerol was interrupted by Thorazine, 100 mg. t.i.d. Of three latent cases treated with BAL, two experienced subjective improvement, whereas a third, revealing only numbness in the distribution of the fifth cranial nerve and dimming vision did not improve.

The improvement in all cases treated was accompanied by normalization of the urinary porphyrin excretion with reduction of the coproporphyrin excretion, by an absence of uroporphyrin and slight residual porphobilinogen excretion in several and by an absence of porphobilinogen excretion in others.

ACTH, administered 15 mg. daily by slow intravenous drip for four days, was successful in reversing the course of one case who had deteriorated under BAL administration (Case II). An additional case responded poorly to BAL therapy but prompt relief with ACTH occurred.

The case previously reported[1] and an ad-

From the Department of Neuropsychiatry, University Hospitals, University of Wisconsin Medical School, Madison, Wisconsin.

ditional case with grand mal seizures and a downhill course failed to respond to ACTH administration but became rapidly asymptomatic following BAL therapy.

This report is submitted to confirm the impression that BAL and disodium calcium versenate should be utilized in the therapy of acute porphyria which reaches a mortality rate as high as 90 per cent, especially in those cases demonstrating neurological symptoms and signs. Frenquel, intravenous Procaine and Thorazine also have a place in a symptomatic therapy schedule.

Symptomatology of cases: a classical case of congenital porphyria with predominant hydroa-vacciniformis symptomatology; eight cases manifesting convulsions (four focal in nature); intermittent schizophrenic-like psychosis, five; peripheral neuropathy, four; recurrent abdominal (or back) pain; three; obstipation in ten; tachypnea and tachycardia in most; and hypesthesia in the distribution of the fifth cranial nerve in one. Spinal fluid ranged from normal to elevated protein as high as 80. Only four cases reported an altered urine color, although the urine during acute stages was especially foul-smelling. Barbiturates may have acted as a precipitating factor in six, sunbathing in two, while exposure to "oil base paints" may have figured in five cases, one of which (Case II) seemed to react in a toxic manner to BAL administration. Multiple blood transfusions may have precipitated an attack post partum in one. In all instances, barbiturates, sulfonamides and other drugs were withheld after diagnosis. Seizure activity appeared to respond favorably in four, inconsistently in one under BAL therapy. Five of the cases previously reported included such diagnoses as conversion hysteria, schizophrenia and arteriosclerotic encephalopathy with aphasia. One case (Case IV), submitted to a laminectomy four years ago for the relief of symptoms assumed to be caused by a cord tumor, demonstrated an adhesive spinal arachnoiditis. Cases showing a predominance of abdominal colic often become addicted, as seemed the case in two patients included in this series. Thorazine and intravenous Procaine seem to be effective drugs in these problems.

Discussion (4 Cases)

The occurrence or frequency of acute porphyria is far greater than heretofore expected. The intermittency of abnormal porphyrin excretion, which often may not parallel clinical symptomatology, makes a rejection of the diagnosis of acute porphyria hazardous unless repeated and detailed urinary studies are carried out when such an etiology is suspected. The observation of reddish or brownish urine by patients has not been a rule.

The significance of the porphyrins in animal or in the role of human metabolism is obscure. In combination with iron and/or protein, porphyrins are needed in the formation of hemoglobin, myoglobin, cytochromes as well as in enzymes such as catalase and peroxidase. Uroporphyrin and coproporphyrin are probaly precursors of the "heme" compounds. If it is true that porphobilinogen is biologically responsible for the synthesis of other porphyrins, as intimated experimentally by Bogorad and Granick,[4] then an "enzymatic block" at this transformation level could account for the withdrawal of important metabolites from the nutritional system. In an earlier publication Peters[1] suggested that BAL is instrumental in withdrawing especially zinc but also other heavy metals from the body which could conceivably produce this "enzymatic block." The role of zinc in porphyria had been postulated by Nesbitt,[5] who deducted that it was a zinc deficit that produced clinical symptoms. Attempts to demonstrate altered zinc urinary excretion levels in cases of acute porphyria have met with equivocable results. Urinary zinc excretion was definitely elevated in six cases tested during the acute phase, often eight times higher than the normal excretion level of 0.5 mg. per 1,000 cc. Sumegi and Putnoky[6] observed that lead, mercury, bismuth, copper, zinc, iron, silver and gold caused white rats to develop weight loss, hyperfunction of the thyroid and porphyrinuria.

The abnormal porphyrins are excreted in urine and feces as a zinc metal complex, according to Watson and Schwartz.[7]

The increased level of urinary zinc excretion would suggest that it may be producing an "enzymatic block" in normal por-

phyrin metabolism which is reversed on chelation with BAL or disodium calcium versenate.

On a previous admission Case II had a borderline lead urinary excretion of 0.7 mg. per cent. It is conceivable that BAL, when utilized in the most recent acute attack of porphyria, despite a normal blood and urine lead level, mobilized lead from the bones to produce a toxic erythema multiforme and more severe disturbance manifested by peripheral neuropathy.

It is suggested from our clinical experience that ACTH is to be used if the initial BAL treatment proves ineffectual after five days. If abnormal lead excretion is demonstrated, disodium calcium versenate therapy is indicated. Unfavorable results of ACTH therapy in acute porphyria have been reported by Mellinger and Pearson,[8] while Olson and Stiles[9] suggest that ACTH and cortisone may have precipitated the fatal outcome in two cases of porphyria. Such a fatal outcome despite cortisone treatment is reported by Gilbert, Toupin and Bell;[10] while Goldberg et al.[11] and also Janoff et al.,[12] and Meyer, Nadler and Bloch[13] report cases benefited by ACTH treatment. Watson[14] reported on eight of 15 cases that responded to 3 to 4 days of ACTH therapy. The use of ACTH as well as brief initial cortisone therapy may well have saved Case I, who showed progressive deterioration following initial improvement with BAL therapy until the ACTH was given.

The use of Etamon and Tubocurare has been advocated by Wehrmacher[15] for relief of pain in treatment of acute porphyria. In our experience, Etamon transiently blocks the pain and reduces hypertensive blood pressure in the acute phase but does not alter the course of the intoxication.

Intravenous Procaine administration has been advocated by Grubschmidt[16] and was successful in controlling the abdominal colic pain in one case when Etamon had been unsuccessful.

Neostigmine has been advocated by Gillhespy and Smith,[17] who noted in their case a similarity to clinical myasthenia gravis.

Exsanguination transfusion is advocated by Deparis, Canivet, Dausset and Rossignol[18] in one case in which 95 per cent of the patient's blood was replaced. Our Case IV had her first acute attack of porphyria following severe post partum bleeding, for which she received 2,000 cc. of blood by transfusion.

Electric shock treatment is advocated in acute porphyria by Lemere,[19] also Freeman and Kolb.[20] One of our cases had 52 spontaneous focal epileptic seizures in the course of three days after she was given two electric-convulsive treatments. Saint, Curnow, Paton and Stokes[21] used electric shock treatment in one of their two reported fatal cases. If seizures are already a potential part of the patient's symptomatology, the use of electric-convulsive treatment would seem hazardous. How many cases of unrecognized acute porphyria with psychosis have received electric shock therapy, the etiology having been missed, is conjectural. Schrumpf[3] used BAL in the treatment of congenital porphyria complicated by hydroa-vacciniformis for the reason that BAL therapy had given good response in hemosiderosis following multiple blood transfusions, and because post mortem examination of congenital porphyria cases had shown hemosiderosis, especially in the liver. Schwarz and Moulton[22] reported deposits of yellow pigment in the Virchow-Robin's spaces and in the wall of the blood vessel in several cases of acute porphyria. They described likewise extensive vascular changes in the brain stem consisting of edematous, proliferative and exudative changes, with a most consistent perivascular accumulation of plasma cells and lymphocytes, suggesting an allergic serum edema. There were nonspecific cellular changes in the neurones consisting of edema, chromatolysis, acute neuronal disease, cell sclerosis, especially the so-called ischemic homogenous cell disease. The distribution of the lesions included anterior horn cell, especially mid-cervical, nuclei of the brain stem, dentate nucleus of the cerebellum, the large neurones of part of the putamen and globus pallidus, certain thalamic nuclei, giant cells of Betz's in the motor cortex, neurones of the autonomic ganglia. The authors concluded that the picture suggested a more toxic than a metabolic reaction as a diffuse toxic meningopolio-encephalomyelitis. Kench, Ferguson and Graveson,[23] also Ivers,[24] report anterior horn in-

volvement in their reports.

It should be said that in these cases of acute fulminating porphyria with severe neurological disorder, recovery appears to have been complete despite the initial severity of the clinical picture. The pathological picture described could explain the focal seizures and arachnoiditis of the cord noted in this series.

Since spontaneous remissions do take place in acute porphyria, the question arises as to whether the results of BAL therapy could be ascribed to coincidence, withdrawal of barbiturates or other factors which triggered the disturbance, or to a delayed response to ACTH in the case that received this medication prior to BAL therapy. The immediate clinical response to BAL or disodium calcium versenate therapy in susceptible cases, however, strongly suggests that BAL itself played a significant role.

Conclusions and Recommended Therapy

1. Acute porphyria is not a rare syndrome; abnormal porphyrin excretion may be intermittent; positive laboratory diagnosis is difficult.

2. Symptoms and signs may include: reddish, brownish, highly odoriferous urine (particularly after standing in sunlight for 24 hours); focal and grand mal seizures; cerebral, focal, degenerative changes (aphasia, apraxia); urinary incontinence; hemiplegia; hemianoptic defect; and arachnoiditis of the spinal cord. Tachycardia and tachypnea are often present, also elevation of NPN with hypertension that may give a positive Regitine test.[1] A lowered level of consciousness, toxic or schizophrenic-like psychosis with hallucinations similar in type to that produced with mescaline and lysergic acid, peripheral neuropathy with pain, motor paralysis or weakness, tremor, or myoclonic jerks, abnormal electro-encephalographic findings may be observed. Complete recovery may occur despite severe damage to the central and peripheral nervous system.

3. BAL therapy may be highly effective in doses of 0.5 to 1.5 cc. t.i.d., bringing about clinical recovery and marked improvement or normalization of porphyrin excretion patterns. Increased urinary zinc excretion may be present with a zinc diuresis on administration of BAL or other chelating agents, and normal values for zinc develop after remission. Zinc or other heavy metals may play a role in producing an "enzymatic block" in the porphyrin metabolism. Disodium calsium versenate therapy may have similar therapeutic ability as BAL.

4. BAL therapy may be effective when ACTH and/or cortisone fail to bring about recovery. ACTH in small doses, 15 to 20 mg. in 1,000 cc. normal saline solution over eight hours, may be therapeutically effective when BAL therapy does not succeed.

5. Intravenous Procaine, 500 mg. in 1,000 cc. normal saline solution for several days, may give relief in neuritic pain and abdominal colic, while Etamon has only transient effect. Preliminary BAL therapy may be necessary, however, to insure relief of pain with intravenous Procaine. Cases manifesting severe abdominal colic often develop dependence on opiates, especially Demerol, suggesting addiction. Thorazine aborted the symptoms in one case when intravenous Procaine proved ineffectual during a second attack.

6. Frenquel may be effective in reversing a toxic psychosis but does not affect the visceral pain in acute porphyria.

7. Sulfonamides, barbiturates (especially pentothal, amytal and seconal), amphetamines, cortisone, exposure to heavy metals, oil based paints, undue exposure to the sun should be avoided as well as alcohol. Paraldehyde may be utilized for sedation.

8. Phenobarbital may be necessary for seizure control, although in most cases BAL therapy will interrupt seizure activity.

9. Heroic supportive efforts may be necessary, such as tracheotomy; patients may recover despite a seemingly terminal picture.

Representative Case Histories

Case I (M.H.):

The patient, M. H., age 25, multiparous with one child of two years, delivered a normal infant 6-9-55 in her local hospital. Severe hemorrhage from a cervical tear occurred the day after delivery. She received 4 transfusions totalling 2,000 cc. blood. A week post partum she was discharged from the hospital but returned 6-18-55 because of abdominal pain and nausea, not amenable to relief by opiates. Constipation followed delivery and continued. She was given sedation but complained of dizziness

and thought once that she was "hearing things," perhaps music. On 6-19-55, following nocturnal sedation, she had 13 grand mal seizures which ceased following phenobarbital sedation. Following this she was semicomatose and unresponsive. Porphobilinogen, coproporphyrin and uroporphyrin were noted in the urine, and she was referred to University Hospitals for admission on 6-28-55.

Examination showed her to be confused as to time and place and with lowered level of consciousness. The complexion was a grayish tan. She complained of blurred vision. An ecchymotic region of the right upper arm was noted, but the shoulder and arm were not tender to palpation or manipulation. Suggestive optic pallor OD; lateral nystagmus; tongue midline; reflexes physiologic. Tenderness in upper thigh and lower back where an L.P. had been done. Fecal impactions were felt on abdominal palpation and tenderness without muscle spasm. Electroencephalograph: 1-2 per second 100-150 microvolt waves in all leads with no localization; basic rhythm 3½-5 per second 30-140 microvolt waves with some low voltage fast activity. Electrocardiograph revealed tachycardia, slight depression of the RS-T segments in II, III, V_3 and through V_6. T waves diphasic or inverted throughout. PR, 0.10; QRS, 0.08. Blood pressure 150/110. NPN 37. Thymol turbidity 3 units. Urinary porphyrins: 5+ coproporphyrin; 3+ uroporphyrin; strongly positive porphobilinogen. Urinary zinc excretion, 1.02 mg. per liter.

On 6-30-55 BAL therapy commenced at 0.5 cc. t.i.d. By evening she volunteered that she felt tired but was thinking more clearly. On 7-1-55 her psychomotor depression was greatly improved, and she first complained of shoulder pain. X-ray revealed fracture, right humerus head, with anterior dislocation. The preceding depression of consciousness resulting from acute porphyria had heretofore masked the orthopedic disability. Open reduction was performed 7-2-55, gas-ether anesthesia, with continuance of BAL therapy. Nevertheless, she continued to improve daily. By 7-6-55 abdominal complaints disappeared and ambulation commenced. 7-8-55 the uroporphyrin excretion increased to 5+, and Etamon was given on one occasion for abdominal cramps. On 7-9-55 BAL was increased to 0.7 cc. 5 times daily, and there was no recurrence of abdominal pain.

BAL therapy ceased 7-15-55. Electroencephalograph, 7-20-55, revealed marked improvement: basic rhythm 7-9 per second 10-70 microvolt waves; some 4-6 per second 20-110 microvolt waves; sleep activity normal distribution. She was discharged from the hospital 7-22-55 with instructions to receive BAL in dosage of 1-1½ cc. on consecutive days should symptoms of constipation, pain or lethargy recurr. Porphyrin studies on her mother, father and sister normal. Urinary zinc excretion continued during the administration of BAL and reached normal levels shortly after cessation of BAL therapy.

Follow-up revealed no return of symptoms, although traces of porphobilinogen are seen occasionally on random urine examination.

Case II (J.S.):

Patient J.S., age 25, was admitted to University Hospitals 8-27-54. The diagnosis of acute intermittent porphyria was previously established, September, 1951, at which time he had complaints referable to backache and peripheral neuropathy in the form of right foot drop. Treated at University Hospitals with sodium acid phosphate because of a blood lead level of 0.70 mg. per cent and ACTH, there followed gradual subsidence of acute symptoms, although foot drop and aesthenia did not disappear for 6 months. The patient, a medical student, had two other attacks dating back to 1949. A possible contributing factor was the administration of triple sulfa drugs at the onset during previous attacks. Prior to all including the present attack there had been exposure to paint with interior and exterior decorating.

A week prior to admission the patient on his honeymoon had partaken of alcoholic beverage and developed constipation, dull aching pains in left lumbar area, pain in thighs, left foot drop, nausea and vomiting. Urine dark brown. Urinary examination confirmed the presence of abnormal porphyrins in the urine.

Admission examination revealed a toxic-appearing male; an edematous, ecchymotic area over the left flank from a hot-pad burn; on walking, left foot drop. In bed he would assume the "knee-chest" position for relief of severe back pain, and there was tenderness and muscle spasm on palpation in the left lumbosacral region. Reflexes intact except for absent left ankle jerk. Subjective hypesthesia over the lateral aspect of the left calf and foot.

Coproporphyrin, uroporphyrin and porphobilinogen strongly positive. He was started immediately on 0.5 cc. of BAL t.i.d. as well as Cobroxin, 1 cc. daily and demerol to control back pain. Paraldehyde was given for nocturnal sedation. Until 9-2-54 the patient appeared to improve, although blood pressure remained elevated and abdominal ileus persisted. On 9-2-54 the patient had 3 grand mal seizures; urinary output decreased and he became confused. 9-10-54 there were visual and auditory hallucinations; bilateral weakness of the deltoid muscle developed; extremities became tremulous. There was marked tenderness to palpation over legs and arms. By the 15th hospital day a rash developed over arms and back, representing a Hebra variety of erythema multiforme. There was almost complete anuria, and erythema and edema became more severe. Sodium acid phosphate was administered and several i.v. doses of Disodium Calcium Versenate. His condition continued to deteriorate, and 9-20-54 the patient was placed on cortisone, 50 mg. every 8 hours for 48 hours, BAL discontinued. The following day dermatitis and clinical status improved, although respiratory exchange appeared marginal and oxygen was administered.

On 9-22-54 ACTH in dosage of 15 mg. in 1,000 cc. of normal saline solution over an 8 hour period was administered and repeated for 4 days only. On the evening of the 4th day the patient became apneic and cyanotic. Following artificial respiration breathing resumed and a tracheobronchial toilet was done. Sodium succinate (2 drams t.i.d.) was administered subsequently in an attempt to improve oxygenation and for its effect on the enzyme systems. The patient improved. On 10-5-54 he developed bronchopneumonia and atelectasis of the left lower lobe, for which bronchoscopy was performed several times and aureomycin administered. He continued subcyanotic despite administration of oxygen. On 10-7-54 tracheotomy was performed, and from that time on improvement was continual. He was discharged on 12-12-54. Coproporphyrin and uroporphyrin levels were now low, but porphobilinogen excretion persisted. Physical therapy was continued, and 4 months later muscle chart revealed complete return of muscle function. The patient gained 40 pounds, and there was no return of neuropsychiatric disturbance. The patient could discuss bizarre hallucinatory experiences present during his acute illness, although there were many gaps in recollection. Medication following discharge from the hospital included adenine in dosage of 250 mg. daily for one month and vitamins. Porphobilinogen continues to be present, although coproporphyrin is negligible and uroporphyrin excretion has not reappeared. The patient has returned to full study in the medical school.

Comment: In retrospect it would seem that ACTH therapy should have been used at an earlier date when BAL therapy seemed ineffectual. Administration of intravenous Procaine initially also might have hastened recovery by reducing demerol and other sedative requirements which may have contributed to progression of the disorder.

Case III (M.J.F.):

Patient M. J. F., age 35, was admitted to University Hospitals 10-22-54. In September the patient began driving herself abnormally, kept late hours and ate sparingly. For several days she had the "flu" with recurrent emesis. A grand mal seizure occurred the afternoon before admission. Following the convulsion she was lethargic and vomited several times.

On previous admissions in 1951, a chronic fatigue state had been diagnosed. In 1953 and 1954 she was hospitalized and a brain tumor suspected because of electroencephalographic lateralization to the right temporal lobe. Pneumoencephalogram, 1-9-54, normal. On 6-26-54 she delivered her 7th child.

The patient, a nurse, formerly admitted use of barbiturates and dexedrine. The patient was dehydrated and uncommunicative. An expressive aphasia existed involving anomia, agraphia and apractic disturbance. She was disorganized as to time and place and hallucinating. Reflexes intact with a questionable plantar response on the right. Urine excretion was dark amber in color and odoriferous. Urine porphyrin studies revealed coproporphyrin 5+, uroporphyrin 5+ and porphobilinogen strongly positive. On 10-26-54 at 8:00 p.m. BAL therapy was started in dosage of 0.5 cc., t.i.d. By the afternoon of 10-27-54 the patient was lucid, no agraphia; she could tell for the first time the correct number of children. She complained of occasional "yellow" acotomata and of having had hallucinatory experiences in which she would see her children at play but in Lilliputian size.

On admission urinary analysis revealed a trace of barbiturate. Electroencephalograph: low voltage fast activity and low voltage slow activity and some 5-6 per second 20-70 microvolt waves in all leads without localization. Zinc excretion 0.61 mg. of zinc per 1,000 cc. A/G ratio and blood bromide level normal, urinalysis negative and NPN 45. The patient was normotensive, although pulse repeatedly reached 100-108, etc. Unfortunately, on the day the patient's BAL therapy was begun, the porphyrin excretion in the urine completely reversed and abnormal excretion of uroporphyrin and porphobilinogen did not recur. Of interest is the fact that the patient had been painting with enamel prior to personality change in September. The patient has been followed in the out-patient department, and there has been no recurrence of abnormal porphyrin excretion. Only once, prior to the menses, was there an alteration in neurological status, consisting of a mild dysarthria.

Comment: The reversal of abnormal porphyrin excretion just prior to initiation of treatment throws doubt on the role of BAL in her recovery and demonstrates the necessity of prompt and perhaps repeated urinary evaluation for abnormal porphyrins should the diagnosis be entertained. Clinical recovery did not precede BAL administration and was especially prompt following therapy in contrast to previous hospitalizations for similar disturbances when recovery was long and tedious.

Case IV (J.F.H.):

Patient J. F. H., age 30, entered University Hospitals 4-20-54. At home narcotics and barbiturates had been given to control pain present from head to foot. Semicomatose and disoriented, she thought she was in New Mexico and had just given birth to twins. Blood pressure, 140/100; pulse 92. Acetone breath. Eyes showed roving movements and lateral nystagmus. Pupils dilated, equal, react to light and accommodation. Funduscopy negative. Neck supple. Abdomen distended; fecal impactions palpable. A Foley catheter was in place, and paraplegia in extension was present with Babinski signs, bilateral ankle clonus and flexor withdrawal.

Past medical history indicated frequent emesis when emotionally upset as a child. In 1945 hemorrhoidectomy was performed with spinal anesthesia, following which she complained of stiff neck, back and leg pains and severe headache. Subsequently she had 2 pregnancies, during which symptoms improved but pain recurred after birth of each child. She was nervous, easily upset, and her hands were often tremulous. Because of weakness of the lower

extremities, positive pyramidal tract signs and sensory disturbance over the L-5 segment, laminectomy was performed elsewhere in 1950 from L-2 to D-9. A red plastic exudate had been seen encompassing the cord, restricting it and the cauda equina. Following surgery the patient was paraplegic with paralysis of bladder and rectum. Surgical re-exploration the same year revealed myelomalacia.

Because of dark brown, odoriferous urine and mental status similar to previous cases of acute porphyria, urinary studies were obtained and reported 5+ coproporphyrin, 5+ uroporphyrin, and porphobilinogen strongly positive. BAL therapy, 0.4 cc. t.i.d., was begun on 4-23-54. The next day uroporphyrin 4+ and porphobilinogen negative. 4-26-54 uroporphyrin and porphobilinogen were negative and remained so. Coproporphyrin remained positive, but the titer progressively diminished. After initiation of BAL therapy her mental status quickly improved, and by 4-28-54 she was mentally clear. BAL was discontinued 4-28-54. Complaint of chest pain was controlled with 1 cc. daily doses of Cobroxin. The sensory level was noted at D-11 on the right and L-1 on the left. On 5-4-54 the patient again became disoriented and had recurrent grand mal seizures. Paraldehyde and sodium dilantin were administered without improvement, and seizures continued. On 5-7-54, despite the fact that uroporphyrin and porphobilinogen tests were negative, BAL therapy was resumed. Seizures promptly ceased and mental status became normal.

The patient was discharged on 5-21-54 and readmitted for several days 6-14-54 because of paraldehyde habituation. Thereafter her family doctor continued twice weekly injections of 1 cc. BAL in addition to B_{12} injections. One exacerbation of severe pain with emesis followed use of zinc oxide ointment as "lubricant" in manual removal of fecal impactions by the husband. BAL dosage was increased temporarily and symptoms disappeared. Some improvement in voluntary movements in the lower extremities and standing with assistance for the first time in 3 years took place. She continues BAL injections, 1-2 cc. per week and occasional Cobroxin injections.

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Psychiatric Horizons and Internal Medicine

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In the vast fields of psychiatry and internal medicine, the problem of psychoneurosis is almost too great for psychiatrist or internist alone to handle. Cooperation between the two is essential if anything is to be accomplished. Therefore, I wish to discuss an internist's view of psychiatric medicine.

Each of these fields of medicine looks upon the patient from a different viewpoint. Each patient is presented as a painting or portrait, to be analyzed and studied over every square inch of canvas. Like a connoisseur of art, a clinician cannot absorb the entire detail of the subject in a short time. The internist all too frequently seizes upon the most prominent subject presented. Too often, the mood and background are ignored. The psychiatrist, on the other hand, may be so engrossed with interpretation of background that perspective of the subject is lost. Imagine, if you can, a moving picture in which the entire story is told with close-ups of the subject. Heads and faces loom large on the screen, blotting out vistas of clouds, mountains, fields, and trees. Such is the viewpoint of many internists. On the other hand, consider a picture in which nothing is presented in the foreground. The principal actors and all action takes place far in the background with unessential characters surrounding the principals and all dwarfed by the immensity of the background. Psychiatry may be at times too engrossed in background and the subject lost in the shuffle.

The wide open space separating the field of psychiatry from internal medicine has narrowed considerably. Both World War I and World War II contributed a great deal to psychiatry. Ignorance on the part of the internist has probably been a major reason for lack of confidence in psychiatry. Possibly some fault lies with both sides. Many internists have not tried to understand the psychiatric approach to the patient. The internist has been trained to look for what he can touch, hear, see, and discover with his five senses. Other real factors have been overlooked—the feelings, craving, personal relationships and social attitudes. These cannot be comprehended by the senses, but only by understanding. The internist has many times attributed pain, weakness, worry about ulcers, fears of cancer and tumors, to imagination—rather than to the real source of distress, the hostilities, anxieties, guilts, resentments, ambitions, etc. The internist has felt that arteriosclerosis, renal disease, and multiple sclerosis, for example, may be the cause of restlessness, loss of concentration and irritability. He has neglected to look for worries, fears and frustrations. The internist thinks in terms of complex fields of physiology, physics, biology and chemistry.

Psychiatrists, on the other hand, have not made the approach to psychiatry easier for the internist. Few psychiatrists have done anything to establish, as you would say, "rapport," between themselves and their fellow physicians. Some have felt they should not be too aggressive in discussing their chosen field. Internists, at times, are disappointed in the results of psychiatric therapy, and feel they can handle the patient as well without any training in psychiatry. The fact that so many charlatans and cultists have long been tied in with the emotional side of medicine and religion has given psychiatry a rather questionable aspect in the minds of some.

Many internists feel that the question of sex has been overly emphasized and poorly presented. It is very hard for the average internist to find a sex connection with such things as early bathroom training. They wonder, too, about the stress placed upon heredity, constitutional factors, and behavior reactions. It is difficult to blame all the major things that happen in a man's life upon the loss of his sled at the age of six. We wonder, too, about the theories which state that something troubling the mother

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can be transmitted to the baby through the maternal milk. Can the mother's tensions be transmitted to the infant, thus producing anxiety and fretfulness in the baby? Do such things as psychotoxins exist?

History: Mental disorders, including psychoneuroses, are by no means new. The trephine hole has been found often in the skulls of prehistoric men. It has been deduced, and probably rightly so, that these holes were made during life to let out the devils and cure mental disease. More than 2500 years ago Socrates scolded Athenian physicians for not understanding that the body could not be cured without curing the mind. Plato and Paraselsus also recognized the role of emotional and mental factors in disease, but it took centuries to assemble these thoughts into real information which could be applied in a practical way.

Despite long recognition of the complex structures of thought, however, our present knowledge, ideas, and observations in psychiatry do not reach back much farther than a century and a half. Most of our knowledge has been developed only within the past half century.

The Cause of Disease: Disease is a disability, a disorder, a dysfunction of the body or mind, or both. In internal medicine we find among the causes of disease: heredity, defective structure or development, physical-chemical-toxic agents, trauma, infection, exhaustion, new growths or degeneration. Heredity is a primary factor in the development of physical structure, intelligence, energy, temperament and personality. There may be great variation, however, in different individuals within the same family. Defective structure or development may produce not only organic but definite psychic changes in an individual. Physical-chemical-toxic agents may produce not only organic changes, but likewise behavior disorders. Trauma, infection, exhaustion and tumors may so upset the normal mental balance of an individual as to mask the presence of organic disease. With increased span of life the degenerative complications of age play a more important part in producing behavior problems. We have saved a large group of individuals from acute infections only to see them fall prey to the degenerative problems which accompany the aging process. Whatever changes occur in the older age group, they are less readily reversible, more constant, and more deleterious in their effects than in younger individuals.

In psychiatry the etiologic factors of disease are stresses, experiences, environmental situations, disordered personalities, insecurities, interpersonal relationships, feelings and emotions. All of these can so disorganize the mind, nervous system, and behavior of an individual as to produce excessive anxieties, fears, resentments, hostilities, depressions, jealousies, hates, delusions and hallucinations. All psychogenic or emotional disorders can produce symptoms characteristic of organic disease. Emotions making a heart light or heavy may account for symptoms referred to the heart region, but without organic heart disease. The difference and intensity of reactions from person to person in the same environment or circumstance depends upon inherited characteristics and response to past experiences.

Neither the internist nor the psychiatrist can accept the old time view that disease consists in a localized area of tissue damage, whether it be caused by injury, bacteria, mechanical or chemical processes. Claims of psychiatry that organic disease is the result of psychogenic imbalance cannot by any means be proved; nor, on the other hand, can the internist maintain stoutly that all organic disease has not had some foundation in an emotional imbalance. In my particular interest in diabetes I have never once been able to satisfy myself that an emotional conflict had a causative effect in this disease. This observation has been supported by several others. Nevertheless, I have read of amazingly close approximations of stress to this disease. On the other hand, in arthritics I have noticed many times that an onset or flareup of the disease would follow some acute strain, and particularly has it been noticed in younger individuals who, for example, were studying hard for college or medical examinations.

Diagnosis: An internist who is called to see a patient with a peptic ulcer knows well that he must seek certain recognizable signs and symptoms, if he is to confirm his original impression and make a diagnosis. Occa-

sionally, it may be necessary to make a diagnosis by exclusion. The internist, however, must be taught how to make a diagnosis of psychoneurosis, just as you do by recognizing definite characteristics of abnormal behavior. It is difficult for an internist to take a routine history without becoming aware of certain factors in the emotional status of the patient. After a patient has a disease for some period of time his complaints are seldom entirely somatic or entirely psychic. The physicion must determine which predominates. A patient may be ill mentally because of an organic lesion, a neoplasm, anemia, vitamin deficiency; or the symptoms of organic disease may be simulated because of psychogenic or emotional imbalance.

We have all heard of the "psychoneurotic" who died of a brain tumor; or on the other hand, of the woman who had five or six operations searching for organic disease—only to be freed of her symptoms when the proper diagnosis of psychoneurosis was made. Therefore, internist or psychiatrist must realize that a patient is a person who represents the resultant of a number of factors—sociological, physiological, psychological, environmental, economic, and finally biological factors—all playing some part in the etiology of the disorder, and all contributing to bring the patient to the physician.

Treatment: It would be well for us to realize that neither the psychiatrist nor the internist can produce miracles. Psychotherapy in the hands of a trained individual can produce astounding results in some cases, only fair results in others; still in some few cases, no results at all. An individual with a psychoneurosis may at times be helped more by the psychotherapy of an internist, because of the stigma so often attached in the minds of some to consultation with a psychiatrist. Undoubtedly, on the other hand, psychotherapy can be of immense help in treating a patient with organic disease, such as hypertension, peptic ulcer, asthma, arthritis, diabetes, etc. We do not imply that these conditions are psychogenic in origin. We mean only that psychotherapy, when properly used, is a powerful adjunct in the overall treatment of disease. To improve an abnormal mind or body, we must use not only internal medicine, surgery, and psychiatry, but physiotherapy, occupational therapy, or any other reasonable therapy. In some instances rather radical procedures such as lobotomy must be part of our armamentarian.

General medical treatment must be instituted to bring the patient to the utmost state of physical well-being. Bad habits of smoking or drinking should be corrected. Excesses, whether good or bad, should be leveled. Adequate rest and a good diet is essential, as well as medications to combat anemia, vitamin deficiency, infections and endocrine imbalances.

Psychiatry then must work through interviews, medication, psychotherapy, psychoanalysis, insulin and electric shock therapy, group therapy, etc. The improvement and spirit of well-being the psychiatrist is able to produce in an individual with organic disease serves as a reminder of something that is too frequently overlooked—that is, we are dealing with a person living in association with others and not simply an organ. We are not dealing with two cubic centimeters of ulcerated gastric mucosa; nor a few ounces of heart muscle with a thrombosed blood vessel; but we are dealing with a person, of whom that tissue forms a part.

Prognosis: The problem of psychoneurosis existing as a single disease entity, or as a complication of an organic disease, presents an ever increasing challenge to the physician today. The internist has to a great extent failed to comprehend the immensity of the problem, although every practitioner admits that the problem exists. Too often the general practitioner or internist shrugs off the psychoneurotic patient with the appellation of "psycho," or hypochondriac. The future of psychiatric medicine, therefore, lies to a great extent in educating the general practitioner and internist how to recognize and treat the psychoneuroses. All psychoneuroses do not by any means require treatment by a psychiatrist. The family physician with a good basic knowledge of psychiatry can help immeasurably with this problem. Therefore, the extension of education is a primary goal for the future. Prevention of psychiatric disorders, too, is a problem of education which will require a searching study and understanding of prevailing cul-

tural and moral patterns. Individuals must be taught to adapt to these changing patterns and conditions as they arise. Child psychiatry is at last receiving more thought and consideration, but much remains to be done in this field. The young child and the adolescent are passing through periods in which progress is promoting changes from year to year far faster than the world progress in other days from century to century. More training is needed for these children in adjusting to these changes, so that nervous and emotional disorders may not develop. Psychiatric examinations in schools will be of great advantage, and parents should be educated to recognize in the early stages any abnormal behaviorism.

Summary: I have endeavored to demonstrate the viewpoint of an internist on psychiatry as we see it today. Both the internist and the psychiatrist are traveling side by side along a road toward a common goal. Neither field can claim success to the exclusion of the other. Patience and understanding are necessary on the part of both.

A Review of the Newer Drug Therapies in Psychiatry

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Reference to the psychiatric literature of the past year leaves one in no doubt that the chemotherapy of mental diseases has come of age. The use of drugs in psychiatry is hardly new; scarcely a year having passed by in the last two decades without the introduction of some chemical designed to relieve mental symptoms. What then is so striking about our present interest in drugs? It is, that in the first instance in the space of two or three years there have been published in excess of two thousand articles on chlorpromazine and reserpine; and in the second, that considerable uniformity of opinion about these drugs is expressed by members of a specialty noted chiefly for its disagreements.

No one of the newer drugs approaches the therapia magna. Some of them, however, do appear to represent major advances in the management of disturbed patients, in the relief of unpleasant symptoms and perhaps in some cases, in the actual resolution of illness. Some of them bid to catalyse new approaches to the understanding of cerebral function.

It is not intended that this paper shall provide an exhaustive review of the recent advances in psychiatric chemotherapy. The subject is still too complex and controversial. The successful introduction of chlorpromazine and reserpine has given a tremendous impetus to the chemical treatment of mental illness. Scarcely a week goes by without a new compound or a variant of an established one being submitted for investigation. As a result, the situation is rapidly becoming so chaotic that even a specialist in the field grows befuddled. Methods of communication in psychiatry have always been poor. We do not have the background of experimental methodology enjoyed by other branches of medicine and our training has rarely included much pharmacology or biochemistry. We are largely dependent on the pharmaceutical houses for our information and it is to their credit that they have not taken advantage of us. Even they do not feel completely secure, for the correlation between the effects of drugs upon the behaviour of experimental animals and that of our patients is not as great as we would like.

The author will now draw largely upon his own experiences with them in commenting upon some of the new drug therapies.

Chlorpromazine was the first of the so-called "tranquillizing" drugs to become popular, though some of its chemical relatives now being investigated (phenergan, parsidol) had been utilized before for different purposes. Chlorpromazine owed its introduction into psychiatry to the fact that it potentiated barbiturates, a phenomenon now recognized to be inconstant in man. In the space

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of three years it has become one of the most widely used drugs in medical practice. Broadly speaking, it is used in psychiatry in three ways. Firstly as a mild sedative for the multitude of patients with neuroses, psychosomatic disorders and situational reactions. Secondly a chemical restraint for the disturbed and excited psychotic. Thirdly in more intensive dosage it is given in an attempt to abolish psychotic symptoms. The literature suggests many other indications for chlorpromazine too, but most of these can be fitted into one of the three categories above. Some facts are clear about the drug. It is not a euphoriant. It does not appear to have the addictive qualities of the barbiturates and withdrawal symptoms are unknown. The sedative and hypotensive effects are only rarely absent. The margin of safety is extremely great. Good effects have been reported with doses of 15 mg. to 4500 mg. per day. Chlorpromazine has a spectrum of biological activity paralleled by few other drugs, and hence has many side effects. This activity appears to be shared by many phenothiazine derivatives in varying degrees and we may confidently expect to see relatives of chlorpromazine put to therapeutic use in the future.

Reports on the therapeutic efficacy of chlorpromazine are sharply divergent. On the one side there is talk of reducing the schizophrenic population in the state hospitals by 25% or more; on the other, statements that good results are meager and transitory. The bulk of opinion, however, tends to suggest that chlorpromazine is an excellent inhibitor of overactivity and mental confusion. Excellent because it is effective, does not impair consciousness, increases appetite, and is simple to administer.

There is no doubt that it is effective in allaying anxiety and reducing tension in the neuroses. European findings in regard to the obsessive-compulsive states have not been found generally true in this country, however. Behavioural disturbances in children have responded well, often dramatically. It is worth mentioning that children tolerate chlorpromazine very well. While most workers view the drug as a symptomatic treatment or as an aid to psychotherapy and other measures, a number of workers including the author, believe that intensive treatment with large doses actually modifies or interrupts the course of some types of schizophrenia. Following the period of intensive dosage an indefinite period of maintenance on a smaller dose is commonly necessary. It seems that in these cases the individual's capacity to react psychotically is inhibited even though his inability to deal with his life situation may persist. Indeed in experiments with monkeys designed to produce chlorpromazine parkinsonism, the author has found that immature animals show very little response to the drug aside from sedation and lessened drive.

There is not time to discuss the various lines of research about the action of chlorpromazine upon the central nervous system. Alteration of function of the reticular system and hypothalamus has been demonstrated in animals, and in one human fatality pathological changes were present in these areas.

The complications of chlorpromazine therapy have been exhaustively dealt with in the literature. At this same meeting last year, the author presented his ideas upon this subject. It is important to distinguish between complications such as jaundice, dermatitis and agranulocytosis, and concomitants of the actual therapeutic action of the drug such as hypotension, lethargy, hormonal changes and parkinsonism. The incidence of jaundice varies from .1 to 3% in different parts of the country. It is possible that the higher figure contains cases of jaundice unrelated to the drug. Jaundice and agranulocytosis are presumably the same sorts of idiosyncratic response seen with other drugs such as thiouracil and methyltestosterone. They are not related to dosage—in fact, seem to occur more frequently with minimal dosage. The only positive sign of overdosage with chlorpromazine known to the author is a toxic-confusional state.

A clear understanding of the side-effects of the newer drugs is very essential to the practising physicion. These drugs bring about drastic changes in the function of both central and peripheral nervous system in addition to the idiosyncratic responses. For this reason they require careful prescription. It is scarcely justifiable to relieve a mild ten-

sion state or stomach upset at the expense of several months of jaundice.

In summary, chlorpromazine is a drug with a wide range of safety but with widespread effects upon the organism. It is often effective in relieving anxiety. It is the most useful inhibitor of psychomotor excitement yet discovered. In larger doses it may block the manifestations of schizophrenia. Depressive illnesses are not usually helped by the drug though the author has secured good results in these cases with energetic administration. In some instances, chlorpromazine may precipitate depression. Indiscriminate usage of chlorpromazine may be attended by unjustified morbidity.

Reserpine was introduced in this country shortly after chlorpromazine. It is a drug of ancient lineage being an alkaloid isolated from the Rauwolfia root used as a sedative in the East for centuries. Despite the fact that it bears no discernible chemical relationship to chlorpromazine its effects on abnormal behaviour are generally similar. It, too, is a sedative and an inhibitor of psychomotor excitement without significant effect upon the brain cortex. While differences in the effect of the two drugs upon the reticular system has been demonstrated, both produce parkinsonism. Reserpine occasionally causes convulsions which is in keeping with animal experiments. Chlorpromazine lowers convulsive threshold in some individuals while raising it in others. In animals the latter drug is an anti-convulsant.

Reserpine, in the author's experience, has a rather unpredictable onset of action. Oral medication frequently does not produce effects in the patients until several days have elapsed. This is sometimes true with intramuscular injection. Sedation with reserpine is not so marked as a rule as with chlorpromazine, though ambulatory patients on roughly equivalent doses of the two drugs often complain more about the lassitude associated with reserpine. The hypotensive response to reserpine is milder and more prolonged. Patients rarely complain of dizziness. Reserpine has not been implicated in the production of jaundice, and idiosyncratic responses (dermatities, edema) are less frequent. In large doses parkinsonism is a very frequent occurrence with reserpine (about 50% in the author's cases). Both drugs have a tendency to increase or produce depressions sporadically especially in neurotic and hypertensive patients. With reserpine, however, the depression may be severe necessitating hospitalization and electroshock. The author has seen three such cases.

There is as yet a paucity of reports examining the relative merits of the two drugs. It is the author's impression that the majority of psychiatrists active in the field favor chlorpromazine over reserpine for psychotic patients. The author now rarely uses reserpine in this type of patient because of unpredictability of onset of effect, liability to depression or increased tension, and relative lack of effect upon basic psychotic behavioural patterns. In the neuroses and in children's behavioural disorders there is apparently little difference between the two agents, though the author again favors chlorpromazine for its more positive action.

Combinations of the drugs have been tried. Better results in psychotic patients with fewer doses of either drug and fewer side effects have been noted. The author has secured good results in a number of manic and schizophrenic patients resistant to either drug given singly. However, side effects were increased. The value of a combination of two novel and inadequately evaluated compounds must be largely speculative at this time.

From among a large number of compounds studied for analeptic properties two have been selected for clinical use because of the low toxicity. Meratran and Ritalin have essentially similar action and comparable to that of amphetamine. Chemically they are both piperidine derivatives. Both are central stimulants with a less vigorous action than that of the amphetamines. Neither is said to be accompanied by overactivity of the sympathetic nervous system. In the author's series of patients this has been generally true though occasional patients have developed autonomic symptoms. Neither drug causes anorexia. They share an antidepressant action though in the author's experience this has only been consistent and substantial with depression resulting from reserpine or chlorpromazine. Results in re-

active and endogenous depressions have been fair but not superior to those obtainable with amphetamine. Both have a tendency to increase anxiety where it is already present, sometimes to an alarming degree. This is probably an unavoidable property of any stimulant drug. However, in a few instances the drugs have had a paradoxical calming effect in anxious patients. Meratran is reported as being effective in the treatment of certain tics. Given intravenously by the author it has induced a conspicuous though temporary reduction of drug-induced parkinsonian symptoms.

It may be concluded that both Meratran and Ritalin possess the desirable effects of amphetamine with fewer side effects. In addition, Meratran may have a more specific effect upon certain conditions associated with muscular hypertonus.

Frenquel, the next drug to be discussed, is remarkable in that its empirical formula is the same as Meratran. It differs in that the piperidyl ring is substituted at the 4 position instead of the 2. In experimental animals it tends to antagonize the action of Meratran, i.e., it is a tranquillizing drug. In normal human subjects in substantial doses the drug is without discernible pharmacological effect. Fabing, however, has demonstrated that it readily inhibits the development of psychotic response to Lysergic acid diethylamide or reverses the response once it has occurred. On the basis of these experiments Frenquel has been used in the treatment of a wide variety of psychiatric conditions. There has been a wide divergence of opinion among investigators about its usefulness. Some have claimed excellent results with deliria and acute schizophrenia; others using small doses over longer periods have secured results in more chronic psychoses. The author has obtained poor results with all schizophrenics though admittedly has not given the drug over long periods. He has obtained results comparable to those achieved with chlorpromazine in some cases of toxic-confusional psychoses. The compound appears to be without side effects. Judgment must be withheld at this time.

The last drug to be reviewed is Meprobamate, otherwise known as Miltown or Equanil. Meprobamate is chemically related to Myanesin and has generally similar properties. It has, however, a longer duration of action, is less toxic and produces greater muscular relaxation and has some anti-convulsant action. While it has been described as a "tranquillizer" it has quite different effects from reserpine and chlorpromazine, and is without significant effect on the autonomic nervous system. In two published studies good results were noted in a variety of patients—mostly in the neurotic category. The author in a double-blind controlled study with 30 mixed neurotic patients has been unable to detect any significant improvement attributable to Meprobamate. It must be said, however, that several patients with symptoms of occipital tension and low back pain have responded to the drug very satisfactorily. A number of severely agitated psychotic depressions responded to Meprobamate in large doses by a lessening of agitation though the depressive affect was unaltered. Side effects include mild dermatitis and excessive sleepiness.

It would be premature to draw conclusions, but the author's present opinion is that Meprobamate has the same order of effect on psychiatric patients that barbiturates do with the addition of a more specific muscle relaxation. It should be useful in conditions associated with much muscular tension.

The science of predictably influencing human behaviour by the use of drugs influencing the central nervous system is making great strides. Experimentally we can produce and abolish psychoses at will. The substances discussed above are but the early forerunners of a whole host of compounds. The need for effective screening techniques, standardization of terminology and improved communication among psychiatrists is urgent.

We must not expect too much of these drugs for human behaviour is more than a biochemical process. Let us not, however, underestimate either their power to do good —and harm if given without due care.

Concept of Assurance of Illness Reversibility

(With Hypnotherapy Case Illustrations)

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In a setting of several approaches to psychotherapy, some involving the use of hypnosis and others completely non-hypnotic, the writer has gained the impression that certain patients are specifically seeking assurance of the reversibility of their illnesses, and having so assured themselves they have reached, for a time at least, the termination point of treatment contact. With some patients, this goal in treatment is not very clear and can only be suspected. In the case of others, the process is more or less apparent. It warrants further study and clarification. Certain hypnotherapy studies seem to elucidate this issue fairly clearly and for this reason brief data are presented now.

Case Histories

Patient 1. This patient was a bachelor in his middle forties. He wanted relief from chronic, troublesome gastrointestinal distress which required care and attention to eating habits in order to allay physical discomfort. He was shy and inhibited, with markedly restricted social contacts. His feeling of inadequacy prompted fault-finding attitudes toward domestic social structure by which he implied he was victimized. He had been in analysis elsewhere for a long time and complained about its ineffectiveness but was capable of an occasional yet begrudging admission of some return when his experience was discussed more fully. He wanted no further analytic approach, however, and set his sights on simple and direct symptom removal. Even limited probing and certainly a more inclusive investigation were not for him. Despite these assertions he engaged in repeated self-initiated but obsessive accounts of his previous experiences, problems and critical judgments. He had been through a number of apparently thorough medical investigations which were neither reassuring nor productive, and medications had been essentially ineffective in satisfying him and relieving his discomfort. A basically time-limited symptom-reducing hypnotherapeutic approach was what he wished. His goal was verbalized quite forcefully in a pseudo-aggressive and loud manner which belied his feelings of weakness and dependency.

Despite his expressed wishes, the patient was able to accept the non-hypnotic contacts prior to hypnotic induction and spoke plentifully, although complainingly. He was satisfactorily cooperative with hypnotic induction technique. Following initial work with hypnotherapeutic approach he was not hesitant to reveal any lack of improvement. Then a point was reached when specific inquiry had to be made of him about degree of progress if any. Only after such inquiry was there hesitant but positive declaration of some symptom relief. Shortly thereafter, the patient terminated treatment alleging that he wished to seek help through routine medical channels, although as mentioned above, several extensive medical studies and treatment attempts had been of no assistance.

Patient 2. A divorced woman in her fifties was employed in a beauty salon. She claimed that she functioned efficiently at her work except that she was slow. As a result, she would be suitable for shops that were not busy, but was concerned about working in busy salons or in others during certain busy hours of the day. She feared being discharged. She would try hard but ineffectively to increase her speed. Although she possessed other financial resources, her ability to work was important for her psychologically. An example of the time-problem was that operations which she might be able to do in forty minutes, should be accomplished in no more than thirty minutes. Other workers would do the same work in twenty to twenty-five minutes and with many customers on hand the total effect over a period of hours was significant. It just seemed impossible for her to cut down on her time. Aside from this specific concern for which the patient requested hypnotherapy, she described difficulties she had had with a paranoid schizophrenic husband and current difficulties with her daughter. She made arrangements for treatment which appeared satisfactory in all respects including financial.

There was nothing unusual in the patient's reactions to hypnotic procedure. A therapeutic technique was employed calling for the patient to engage during hypnosis in visual imagery of the scene visualization type in which she would view herself engaged in the very work which she was concerned about. While so engaged she would find herself operating quite efficiently. She would allow for passage of time and would experience its hypnotic modification in a way that would result in her accomplishing her tasks more rapidly than usual.

Shortly after the onset of treatment and long before any beginning results would ordinarily have been anticipated the patient was discussing again some personal issues without reference to her work problem. Simply as routine, the question was put to her about it and only then did she reveal that she had been able, following the hypnosis work, to

cut down her work time from forty minutes to twenty-five. Soon afterwards, in rather matter of fact fashion and with no complaint, she claimed she found it necessary to discontinue treatment for financial reasons, quite in contradiction to her originally expressed ability to undertake treatment just a short while earlier.

Patient 3. After the previous patients and others who appeared to reflect similar reactions had been seen, another patient was studied. She supplied what seemed to be corroboration of impressions which had already been gathered.

This patient sought hypnotherapy for relief of hot flushes which were part of a menopausal period. She was not sufficiently satisfied with previous medical and psychiatric contacts. She felt that people noticed the reddening of her face which increased her shyness, insecurity, and self consciousness. She lacked confidence in herself. Her work was selected on the basis of hours which would bring her into minimum contact with other people. She believed, correctly, that she looked distraught. She was not free in her contacts with people. When she flushed she felt anxious, the sensations were uncomfortable and she felt that others could see what she was experiencing. Although quite sensitive in her relations with people, she evidently worked efficiently.

The hypnotherapeutic approach consisted essentially of two parts. One related to symptom relief. The other encouraged improvement in broader aspects of personality functioning. The latter incorporated a modified analytic type therapy and the patient was able to achieve meaningful insights and to integrate significantly a variety of past and present experiences. The symptom approach responded to induction of altered sensory experience stressing ability to eliminate sensation from conscious awareness and to experience sensation without concurrent discomfort or disturbance. Allowance was made not only for the possibility of decreasing symptoms, but also for permitting appearance of what might fall into the range of normal physiological occurrences while diminishing the intensity of adverse psychological response to such occurrences.

The patient responded increasingly to treatment and expressed satisfaction with progress. Then she had the need to cancel or postpone certain sessions, but alleged reasons appeared suspect. Since there was no decisive termination at this point it was possible to discuss with her the suspected attempt to withdraw prematurely from treatment. It was at this time that the patient spontaneously and unexpectedly confirmed what the therapist had surmised to be true for other cases. She claimed that she believed she had proved to herself that she was able to improve and to get well and that her symptoms need not continue unabated. Having demonstrated this to her own satisfaction she said she was tempted to discontinue.

Discussion

The first question that arises about the reactions described, is whether they fall under the more general problem of secondary gain from symptoms and the influence of such gain on improvement or failure, as well as on other aspects of the therapeutic contact. It seems that the larger issue of secondary gain is involved, although this particular type of behavior may well qualify as a reaction distinct in itself and relatively circumscribed with some special characteristics. For example, this assurance of illness reversibility seems to be a goal in itself. Once achieved, a break in treatment is likely to occur. This termination may take place almost immediately after the start of treatment, or it may be delayed for an indefinite period. There must be improvement first, and there must be a degree of improvement, whether small or great, which is sufficient to assure the patient of reversibility. Whereas the specific area of desired improvement is clearly outlined by the patients when seeking help, reference to such improvement is usually not verbalized spontaneously by the patient when he has arrived at the crucial point of anticipated termination. It is clarified through deliberate or chance questioning by the therapist. If there is no improvement, a patient often complains about lack of results. There are usually no such claims or complaints at the termination point in the type of patients showing the reaction emphasized now. Reasons offered for termination are often inconsistent with information previously offered by these patients. Thus, shortly after making apparently suitable financial arrangements, finances may be used as the reason for discontinuing. The desire for another type of therapy may be volunteered as the reason, whereas the patient had previously claimed failure with the very type of study or treatment he now alleges he wishes to seek. Termination is usually decisive. When stated during an interview, the reasons may be such that the therapist deems it unfair to question them or unethical to persuade. Otherwise termination may be by telephone with deliberate avoidance of discussion. Thus, it was the opportunity to discuss the problem which resulted in spontaneous confirmation of these impressions by the third patient described here.

The writer is of the opinion that this type

of reaction is widespread in most areas of medical practice and that it has been observed frequently. The opportunity to clarify it and offer a more precise description seemed to be aided by the sharp delineation of time factors supplied by response to hypnotherapy in these cases.

Summary

Some patients appear to harbor the major goal in treatment of assuring themselves only about the reversibility of their illnesses. This specific goal may be viewed as part of the larger problem of retention of symptoms for secondary gain. With the goal achieved, treatment is terminated. This may occur soon after it was started or it may be delayed, but some degree of improvement must take place first. Areas for improvement are clearly outlined by the patients but improvement at the point of termination is usually not verbalized spontaneously. Reasons given for discontinuing treatment are inconsistent with information volunteered previously. The need for this assurance of reversibility of illness and its role as a goal in itself, followed by termination of treatment, is probably widespread in most areas of medical practice. Its existence as a relatively circumscribed phenomenon requires further description and elucidation. Current presentation is made possible as a result of rather precise illustration in the hypnotherapy cases described above.

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The Effect of Lysergic Acid Diethylamide on *Betta Splendens:* I.

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In 1954 Abramson and Evans[1] reported that immersion of juvenile *Betta splendens* (Siamese fighting fish) for six hours in 100 cc. of water containing as little as 0.5 micrograms per cc. of LSD-25 resulted in a characteristic alteration of motility. Later they found that the monoethylamide of lysergic acid (LAE-32) had qualitatively the same effect.[2]

The remarkable properties of LSD-25 in the human being have so far been difficult to relate to phenomena in non-human species. Specific effects have been reported only in certain spiders by Witt[3] and in waltzing mice.[4] Our own fruitless search for specific effects covers observations made between 1952 and 1954 on bacteria, amoebae, paramoeciae, annelids, molluscs (both of fresh and salt water), crustaceans, a few insects and tadpole larvae. It can only be said that LSD-25 exerted no evident action on any of these organisms except at such high concentrations (over 10 micrograms per cc.) that the unique action of LSD-25 would be questionable. A single exception is the snail, *Ambularia cuprina* (Abramson and Jarvik[5]).

An understanding of the sites and mechanisms of action of LSD-25 is of the greatest importance for the light which might thereby be thrown on the schizophrenic psychoses. The very slight action of LSD-25 on the hundreds of species which have been subjected to it indicates a highly specific action; its effects on spiders, waltzing mice, *Betta splendens* and on man conceivably have nothing in common. Indeed, it might also be that none of these effects has anything to do with schizophrenia. We are nevertheless justified in searching to determine whether, by assuming relevance, we may learn something of value.

Materials and Methods:

We examined the effects of some 60 pharmacologic agents on 22 species of fish, using the effect of LSD-25[B] on juvenile *Betta splendens* as an investigative hub. The drugs were dissolved in water in concentration starting at twice the maximum adult human dose per 100 cc. and descending to concen-

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trations which exhibited no effect on fish after six hours' exposure.

This report will deal only with observations made on fish treated in the manner described by Abramson and Evans. Usually the smaller fish were immersed in 100 cc. of solution, larger fish in a suitable volume (e.g., 500 cc.) as recommended by professional fish culturists. Water was artesian well or clear fresh pond water which was drawn at least 24 hours previously, so that there was no shock to fish on immersion.

Generally, in addition to untreated controls, no more than two drugs were studied concomitantly. Three or four fish were used in each test immersion. When a drug was found which might have an LSD-25 effect or which might be a blocking agent for LSD-25 it would be studied in a variety of ways: e.g., (1) simultaneous action of the drug and LSD-25, (2) preliminary intoxication with one drug followed by immersion in a solution combining both drugs.

Juvenile specimens of the following species were studied: *Betta splendens, Aequidens latifrons, Aequidens portalegrensis, Molleinisia latipinna, Brachydanio reria, Xiphophorous helleri, Trichogaster sumatrans, Trichogaster leeri, Platypoecilus maculatus, Tanichthys albomibes, Macropodus viridi auratus, Lebistes reticulatus, Pterophyllum scalare, Barbus titteya, Haplochromis multicolor, Pristella riddlei, Carassius auratus, Hemigrammus ocellifer, Corydoras leopardus, Cichlasoma meeki, Corydoras aeneas* and *Barbus sumatranus.* Of many species adult specimens were also tested.

The *Betta splendens* tested varied in length from 8 to 20 mm. from nose to base of tail fin. Our observations included not only those on undisturbed fish but also on rheotaxis, on response to approach of foreign bodies and on feeding behavior.

Experimental Results:

In solutions containing 1.0 micrograms per cc. of LSD-25 none of the fish showed any marked accentuation of normal behavior and no evidence of behavior not characteristic of the species (e.g., no "schooling" in *C. leopardus,* but in *Pt. scalare*).

With regard to the effects of LSD-25 on *Betta splendens* we were able to confirm Abramson and Evans in every detail. The normal *Betta* was relatively inert, however, and if left undisturbed would at times be observed to "hang at the surface," or to curl its body and remain so for some moments, or to swim backwards or sideways. Against a dark background, too, dispersion of melanophores occurred. With respect to these phenomena, LSD-25 could only be said to have produced an exaggeration of normal behavior. The "barrel-rolling," however, had not been observed by us in normal fish at lower levels of LSD-25 (e.g., 1 microgram per cc.). Above 1 microgram per cc., fish would often be seen to lie on their sides, their bodies S-shaped, for minutes on end. Phenomena rarely if ever seen in normals which were prominent even at low levels were the "Cartesian diver" effect and the reduction in motility which Abramson and Evans called the trance-like state. This latter was partly a function of stimulation frequency and intensity. A normal fish would rapidly orient itself in swirling water and would swim with such speed as to remain almost fixed with respect to the wall of the vessel in which it swam. LSD-25 fish oriented somewhat less rapidly and were unable to maintain position as well as would the normal. A normal fish would avoid a pencil lead brought to within 2 mm. of its nose, although it would allow gentle touching of the tail fins. LSD-25 fish would avoid only after actual touching of the nose and would permit being pushed in a circle by pressure on tail, fin or body. Normal fish would rarely permit a wire loop to be passed over themselves from nose to tail, which would touch both their pectoral fins; LSD-25 fish readily permitted this. Avoidance, when it occurred, was by minimal action rather than the normal rapid darting away for a considerable distance. Normal fish unfed for 24 hours would go avidly after finely granulated food. LSD-25 fish seemed to remain unaware of the presence of food for some time (often for minutes), and then might be responsive only to a few pieces settling down. Once started, some fish continued to feed as long as particles were on the surface or were settling. Their aim for food, once they went for it, was good.

It was of particular interest to examine

whether other psychoplegic and hallucinogenic drugs exerted an effect like LSD-25. Most of the species noted above were exposed to mescaline sulfate in concentrations up to 250 micrograms per cc. and to bufotenine[C] up to 100 micrograms per cc. A few were treated with bufotenine 500 micrograms per cc. during six-hour observation periods. No alteration of behavior was observed in any of the species under these conditions. Nor did there appear any enhancement or inhibition of LSD-25 effect.

With *Betta splendens* and occasionally with other species, examination of a number of sedatives was carried out, including paraldehyde, chloral hydrate, dormison,[R] a number of barbiturates, morphine, cocaine, chlorpromazine and reserpine.[C] While moderate doses exerted sedative effects on fish, other effects were variable (e.g., aggregation of chromophores by cocaine, dispersion by reserpine[6]), none of the above-mentioned sedatives exerted an LSD-25 effect, nor did they specifically enhance or block LSD-25 action.

Antihistamines and related compounds (pyribenzamine,[R] benadryl,[R] antistine,[R] trimeton,[R] bonamine[R] were also powerful sedatives on fish, but they did not enhance or block the LSD-25 effect.

A group of agents with autonomic stimulating and blocking properties had no LSD-25 effect and failed to block LSD-25 action. These included ephedrine, neosynephrine,[R] vasoxyl,[R] eserine, atropine, papaverine, artane,[R] serotonin, adrenaline and adrenochrome.

Hyoscine alone of all drugs studied clearly and greatly potentiated the action of LSD-25. In one experiment seven rows of seven columns each of quart Mason jars were set up. Into each was placed 500 cc. of water which had stood at least 48 hours and to each ten gallons of which had been added one quart of sea water. In each jar were placed three juvenile *Bettas*. Twelve hours later all fish were healthy and normally active. At the end of 12 hours, drugs were added. The hyoscine concentrations in the columns were 0.4, 0.1, 0.025, 0.00625, 0.00156, 0.0004 and 0.0 micrograms per cc.

At one hour the limit of definite effect with the two micrograms per cc. of hyoscine was 0.025 of LSD-25; with one microgram per cc. of hyoscine the limit of definite effect was 0.1 micrograms per cc. of LSD-25; with no hyoscine the limit of definite effect was 0.40 micrograms per cc. of LSD-25.

At two hours the LSD-25 effect was evident at 0.00156 micrograms per cc. of LSD-25 with four micrograms per cc. of hyoscine. It was evident in the two micrograms per cc. of hyoscine at 0.00625 micrograms per cc. of LSD-25. At 0.025 micrograms per cc. of LSD-25 the effect was already evident at 0.5 micrograms per cc. of hyoscine. In the absence of hyoscine 0.1 micrograms per cc. of LSD-25 was effective.

At two hours also an effect due to hyoscine alone occurred only at 16 and eight micrograms per cc. This consisted in a tendency to lie on the side quietly either at the bottom of the jar or at the top, sometimes with marked curling of the body. Stimulation would lead the fish to become very active for a brief period in contrast to the minimal avtivity of the fish intoxicated with LSD-25. In addition, the hyoscine reaction differed from LSD-25 in that there was no "Cartesian diver" effect, no backward swimming and no barrel-rolling. Further, undulation of the dorsal and tail fins was not stopped, although the undulatory frequency was slow. The combination of hyoscine and LSD-25 occasionally lead to periods of excitement and sometimes even to fighting in the lower hyoscine combinations.

Further observations were made at three and six hours. There was no marked increase in the manifestations of intoxication during this time. At six hours, indeed, there had been a recession of activity at the lowest level of LSD-25 concentration. The larger doses led to an extreme torpidity of the fish, which would cluster together, sometimes lying on their sides at the surface of the water. On transfer to fresh water the effect wore off slowly during a period of 12 to 24 hours.

With pilocarpine 150 micrograms per cc. an otherwise unobserved effect occurred with *Betta splendens*. About one half hour after immersion, the fish would stand on their heads at the bottom of the jar, their bodies at angles of 75° to 90° to the horizontal.

Their pectoral fins hung limply downward and their backs were arched as in opisthotonos. The effect was of variable duration, often ending in one hour, but at times (as in 300 micrograms per cc.) persisting for 24 hours.

Betta splendens were first intoxicated with LSD-25 1.0 micrograms per cc., then pilocarpine was added to make the solution 150 micrograms per cc. with respect to pilocarpine. Within 10 to 15 minutes the LSD-25 effect had been modified and over a subsequent period of several hours the fish exhibited normal behavior. Now and then a fish might swim head down, but feeding behavior, response to swirling water and to the approach of foreign objects was normal. Fish previously intoxicated with 3.0 micrograms per cc. of LSD-25 transferred to pilocarpine 150 micrograms per cc. showed normal behavior within one-half hour. *Bettas* first subjected to hyoscine 4.0 micrograms per cc., then to hyoscine 4.0 micrograms oer cc., plus pilocarpine 150 micrograms per cc., failed to show the pilocarpine effect.

Lysergic acid monoethylamide (LAE-32) had an LSD-25 action, but this was not shared by ergotamine,[R] dihydroergotamine,[R] methergine[R] or hydergine,[R] nor did these drugs block the action of LSD-25.

Of all the drugs studied, only pilocarpine specifically blocked LSD-25 effect. Hyoscine potentiated LSD-25 and blocked the effect of pilocarpine, but did not in itself alter behavior of the fish up to concentrations of four micrograms per cc.

Discussion

The observer who watches narcotized fish and compares them with LSD-25 fish, recognizes differences in body posture, fine fin movements and in response to stimuli. LSD-25 does not disconnect, as it were, the central from the peripheral nervous system. Fish intoxicated with LSD-25 resemble in many ways trout under tectal stimulation as described by Akert.[7] The impression of alteration, rather than of loss, of muscular tonus suggests a disturbance in the vestibular innervation, a disturbance arising out of alteration of signals, as from the optic tectum. Evarts[8] and Pennes[9] have presented evidence that LSD-25 decreases the height of the synaptic volley in the visual pathways of cats and monkeys. Marrazzi and Hart[10] have shown also that LSD-25 as well as bufotenine and mescaline decreases synaptic transmission in the cat. The thought, then, has been entertained by the writer that the action of LSD-25 on *Betta splendens* could be due to an action on the neurones of the visual pathways whereby the spatial and temporal organization of impulses, which code information to the tectum and thence to other parts of the central nervous system, suffers deformation. If this be indeed the site and the mechanism of action of LSD-25 on *Betta splendens,* might it not also be the site and mechanism of action productive of the psychic effects on man?

With this question in mind, the effect of hyoscine on LSD-25 with fish is especially interesting. It has long been known that tropanes (atropine, hyoscine and cocaine) are particularly potent agents for the production of psychosis with delusions as well as visual and auditory hallucinations.[11,12] It has also been known that synthetic drugs with hyoscine-like action which have been introduced in medicine for the treatment of paralysis agitans not infrequently induce psychosis. While the majority of these psychoses are delirious in nature, some of them seem indistinguishable from acute schizophrenic attacks.[13]

A review of the literature suggests that a synergistic action of hyoscine and other tropanes is much more effective in producing delirium, than is the pure drug alone. This seems to be the case also with LSD-25 and hyoscine—at least as far as our experience with fish is concerned. We can at present offer no theories to account for the synergistic action of hyoscine and LSD-25, nor for the absence of such effect with atropine. Similarly, we are unable to offer an explanation for the action of pilocarpine. Text books assert that pilocarpine acts directly on smooth muscle and on cells of the salivary glands.[14] While it is plausible that this relates to the difference between the action of pilocarpine and of physostigmine on the blocking of LSD-25 effect in *Betta splendens,* how pilocarpine could restore the coding of information, if this be its action, is beyond our conjecture.

Summary

The action of 60 pharmacologic agents has been examined on 22 species of fresh water fish. LSD-25 has a special action on *Beta splendens* which is not found in the other species. This action is partly shared by LAE-32 but not by serotonin, bufotenine, mescaline or adrenochrome. It is potentiated by hyoscine and counteracted by pilocarpine.

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The Effect of Lysergic Acid Diethylamide on *Betta Splendens:* II. Frenquel

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In his initial studies on Frenquel (α-(4-piperidyl) benzhydrol HCl) Fabing[1] reported a blocking effect on the psychic action of LSD-25 in man. On the basis of this we thought that it would be of interest to determine whether it blocked the action of LSD-25 in the Siamese fighting fish (Betta spendens).[2,3]

Preliminary experiments failed to reveal a blocking action but, certain questions having been raised, a more elaborate test was conducted on June 12, 1955.

Materials and Methods:

At 9 a.m. *Betta splendens* of two sizes were placed in LSD-25 2.2 gamma per cc. Smaller fish were about 8 mm. long; larger fish were 20-25 mm. long. Inasmuch as both sizes of fish exhibited the same effects no further distinction will be made between them.

In another container *Betta splendens* were placed in Frenquel 500 gamma per cc.

At 2 p.m. very intense effect was evident in the LSD-25 fish. The fish in Frenquel solution were active; melanophores were constricted.

To permit comparison as to the rate of disappearance of the effect after removal of LSD-25, fish were transferred as follows:

1A—Fish pre-medicated with LSD-25 were placed in fresh water.

1B—Fish pre-medicated with LSD-25 were placed in Frenquel 250 gamma per cc.

To permit comparison as to the rate and extent of appearance of LSD-25 effect, fish were transferred as follows:

2A—Fish previously in Frenquel were placed in LSD-25 1 gamma per cc.

2B—Previously unmedicated fish were placed in LSD-25 1 gamma per cc.

To permit comparison of previously LSD-25-treated fish and previously Frenquel-treated fish in overcoming LSD-25 effect in the presence of both Frenquel and LSD-25, fish were transferred as follows:

3A—Fish previously medicated with LSD-25 were transferred into solutions containing 1 gamma per cc. of LSD-25 and 250 gamma per cc. of Frenquel.

3B—Fish previously medicated with Frenquel were transferred into solutions containing 1 gamma per cc. of LSD-25 and 250 gamma per cc. of Frenquel.

Results

During the first half hour the usual effect became evident in all fish in LSD-25, in that at 2:30 p.m. there was no evidence in any jar of LSD-25 blocking. At 3:30 p.m. 1B fish were paler than 1A. In other words, LSD-25 effect was less intense in Frenquel than in the fresh water. Fish in all other jars showed intense LSD-25 effect. At 4:30 p.m. 1B fish were paler than 1A were at 3:30, but one fish would still cling at the surface, curved into an almost complete circle and others were all quiet. That is to say, that although LSD-25 effect in Frenquel was less than in fresh water, it still was not completely abolished in 2½ hours. All other fish showed strong LSD-25 effect.

These fish were observed at irregular intervals from 4:30 to 9 p.m. The LSD-25 effect in 1B gradually decreased until the fish were normal in color and behavior.

Summary

In fresh water, fish previously treated with LSD-25 returned to normal less rapidly than in Frenquel solution. Other than this, under the conditions noted, Frenquel had no effect on LSD-25 phenomena in, nor did it exert any effect itself upon *Betta splendens.*

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From Research Division, Central Islip State Hospital.

Eastern Psychiatric Research Association Proceedings at Meeting of February 9, 1956

DAVID J. IMPASTATO, M.D., *Presiding*

Should a patient be required to sign consent to have electric shock treatments?

Discussion:

Mr. Isadore Siegel, Assistant Attorney General, State of New York, in charge of Division of Hygiene:

Certain claims of malpractice are hazards peculiar to psychiatry. Many psychiatric patients are inherently litigious. Patients may confuse fact with fancy and fantasy often leads to charges of odd behavior.

The psychiatrist is often called upon to render an opinion which results in the loss of a right or privilege: i.e. a person may be deprived of his driver's license, or his right to dispose of property or even his freedom. Explanations of psychiatric diagnoses to members of the family may possibly lead to charges of slander. The legal problem of consent to a procedure is more complicated in psychiatry than in the surgical specialties and induced convulsions or shock therapy may be malpractice traps.

Operation without consent is a trespass. It constitutes a technical assault and renders the operating surgeon liable in damages. In Schoendorff v. New York Hospital (211 N.Y. 125) the court said,

". . . that every human being of adult years and sound mind has a right to determine what shall be done with his own body; a surgeon who performs an operation without his patient's consent commits an assult for which he is liable in damages."

The unique question is presented as to rights and obligations of the psychiatrist in rendering convulsive shock treatments. The chief concern of society with the topic under consideration arises from the implied contract ordinarily incident to the physician's engagement. A physician in undertaking the professional care of a patient assumes certain obligations. He impliedly contracts and represents that he possesses, and the law makes it his duty to possess, the ordinary degree of skill and learning commonly possessed by reputable physicians in the same general line of practice, in the same locality, or in similar localities; he is bound to exercise ordinary care and diligence in the application of his skill and knowledge to accomplish the purposes for which he is employed; he is obligated to exercise his best judgment, the judgment of a physician; he must act toward the patient with utmost good faith; and it is his duty to keep abreast of progress in the profession and to utilize accepted and recognized methods in diagnosis and treatment.

Unless the patient himself indicates a desire to the contrary, the physician must make a frank and full disclosure to his adult, mentally competent patient of all of the pertinent facts of the case. One who holds himself out as a specialist in the treatment of certain organs, injuries or diseases is bound to bring to the aid of one employing him that degree of skill and knowledge which is ordinarily possessed by those who devote special study and attention to that particular organ, injury or disease, its diagnosis and treatment, in the same general locality, having regard to the state of scientific knowledge at the time. The certified examiner treating a psychotic patient should have training in neuro-psychiatry as well as in shock techniques. Shock treatment cannot be learned from books. The psychiatrists who want to use it should spend weeks or better, months, in studying the treatment at a hospital where it is applied expertly. He must be thoroughly familiar with symptoms displayed during the preshock phase requiring variations in treatment procedures; his nurses should have special knowledge of the treatment; and every requirement to fulfill the treatment to perfection should be complied with.

Shock treatment is like an operative procedure. Just as the surgeon and anesthetist record their observations during operation, the psychiatrist and nurses should record their observations on the physical and mental changes that occur during and after hypoglycemia. A complete clinical chart should be maintained. Accordingly, a psychotic patient, being of adult years and sound mind must consent and grant permission for shock treatment; if the patient is *non compos mentis*, consent must be obtained from one other than the patient, such as husband, wife, father, mother, or whoever stands in the position of guardian of the mentally ill person. While there do not seem to be any cases in point, it would appear that the only circumstances under which a shock treatment could be performed on such an individual, mentally ill, without consent, would be in an emergency where the treatment would be necessary to save life, limb or health.

What constitutes a sound mind must be determined by the psychiatrist. A subject who is mentally ill is not necessarily unsound of mind or incompetent. To constitute one of unsound mind or incompetent, the mental disorder must cause defect in judgment and that defect in judgment, as a practical matter, causes a specific incapacity with reference to the matter in question. There is a distinction between a certification of a mentally ill person to a hospital for treatment and an adjudication of incompetency.

In Finch v. Goldstein, 245 N.Y. at page 303, the court said:

"What is meant in these decisions by 'Office Found' or 'Judicially declared incompetent' . . . Until the appointment of a committee neither the State nor any one else has any power or control over his property or any authority to act in his behalf. He

(the patient) alone remains in possession of his property and can dispose of it. If as a fact he be incompetent at the time he acts, his transactions may be set aside at his election either by himself or by a committee subsequently appointed. His acts before the appointment of a committee are thus voidable, not void."

A patient who fully understands the nature and consequence of his deed or act; who possesses good insight and judgment though mentally ill in limited respects must be deemed a person of sound mind for the purpose of executing a written consent for electric shock treatment.

What constitutes an emergency to warrant Electric Shock

Where the psychiatrist in his best judgment believes that the patient will die, lose a member or be seriously and permanently impaired in health unless shock treatment is administered immediately, then and only then, may the treatment be performed without the consent of someone. The best illustration of such cases are represented by suicidal or homicidal patients or a patient requiring continued restraints to avoid inflicting self bodily harm or injury to others. In these cases, it would be better judgment to obtain confirmation of the psychiatrist's decision that an emergency exists by certification by two other psychiatrists of equal qualifications.

The marital status makes no exception to the rules. The consent of the husband or wife of a patient is not necessary if the patient is of sound mind and knows the nature and effect of shock treatment. Better practice and cautious surgeons and psychiatrists obtain the consent of both husband and wife. In the case of infants the consent of the person in *loco parentis* is required. If the infant has reached the age of adolescent discretion, the consent of the infant should be obtained as well.

If the surgeon or psychiatrist confronted by an emergency, is not to be permitted, after having fairly and carefully examined the situation, to exercise his professional judgment in his honest endeavor to save human life, then the public at large will suffer. If the psychiatrist is not permitted to honestly use his best judgment upon the necessity for shock treatment, without waiting to get the consent of the patient, his parents or next-of-kin, then is the skilled hand and mind of the psychiatrist stayed by an unreasonable rule, often to the detriment of the patient and humanity at large.

Consent, in general, is a mandatory requisite before the rendition of shock treatment. To avoid claims of trespass—claims of assault—monetary judgments for damages—the psychiatrist should obtain proper written consents from those who legally may execute them before electric shock treatments are rendered.

The following are recommended suggestions.

1. Obtain written consent from the patient, if of sound mind, or if incompetent from the next-of-kin and the duly authorized guardian or committee of the person.
2. Be sure the document makes clear the nature and extent of the treatment as well as the risks involved.
3. Obtain corroboration from other qualified physicians, preferably the family physician, on the advisability of the treatment.
4. If possible, have a qualified physician witness the convulsive shock treatment to attest your skill and diligence.

Discussion

Dr. D. J. Impastato, New York City: There is general agreement that a responsible relative of a patient who is going to receive electroshock treatment should sign a consent, irrespective of whether or not the patient signs.

In my practice, I do not ask the patient to sign at all. I feel that asking a patient, who is considered psychotic by the physician, to sign consent for treatment, may turn out to be detrimental should he refuse to sign. He would be deprived of the benefit of the treatment. In a depressed patient this may result in serious consequences, possibly death by suicide. Many depressed patients seek help but they do not consider themselves psychotic. In such patients I feel that it is psychotherapeutically correct to explain to them that they are not psychotic. Since these patients associate electroshock therapy with psychoses, it is not wise to inform them that they are going to receive treatment. For these and other reasons, it is my opinion that it is not good practice to ask a psychiatric patient to sign his own consent.

Thirty three practicing psychiatrists attending the meeting were canvassed as to whether they required the patient, a relative or both to sign a form of consent. Also whether by not having the patient sign, any legal suits resulted. A tabulation of the answers is as follows:

Pt. Only	Relative Only	Both Pt. and Relative	Pt. Occasionally, Relative Always
2*	18**	6	7

*One psychiatrist from a private sanitarium—voluntary patients sign, others do not. Relatives do not sign.

**One psychiatrist from a state hospital—Patients are legally committed for treatment and do not sign.

Book Reviews

DISEASES OF THE NERVOUS SYSTEM: By Sis Russell Brain, Bt. D.M. (Oxon) P. R. C. P. (London), Physician to the London Hospital and to the Maida Vale Hospital for Nervous Diseases. Cloth. $10.50. Pp. 996 with illustrations. Fifth Edition. Oxford University Press, 114 Fifth Avenue, New York 11, N. Y., 1956.

The present fifth revision has appeared after a four-year interval. In this edition of July 1955, the volume is as consistently up-to-date as it is possible to collate the knowledge of so fast developing a subject as neurology. The book retains its classical style and characteristic format so well known since the original work first appeared more than twenty years ago. It contains close to 1000 pages of dependable information, which is authoritatively authored. Some of the chapter material has undergone minor textual changes and entirely new matter has been presented to include cervical spondylosis, the Coxackie viruses, inclusion body encephalitis, toxoplasmosis, polymyositis, and neuropathy and myopathy associated with carcinomas. Among other timely revisions there also appear the recent advances in the treatment of meningitis, poliomyelitis, as well as a new section which includes Papez's neurological basis of emotion and the neural basis of consciousness and unconsciousness. Many of the references at the end of each chapter reflect up-to-date bibliographical revision.

On the constructively critical side, this reviewer would suggest a more comprehensive compilation of the index with cross indexing to make for greater subject-matter accessibility. A few examples of deletions which make for time-consuming search within the body of the text may be suggestively quoted: Psychological aspects of neurology, Kayser-Fleischer ring, ictus, apoplexy, strephosymbolia, status dysmyelinisatus and marmoratus, Stellwag sign, albuminocytologic dissociation syndrome, and many others.

The book contains excellent illustrations and includes a number of well reproduced roentgenograms which have been appropriately chosen for the various intracranial conditions they represent. The subject of neurology is masterfully covered and the book should be in the hands of all concerned with the specialty of the subject, as well as those practitioners and students of medicine in search of a comprehensive treatise on the disorders of the nervous system and their clinical approach.

Lewis J. Siegal, M.D., LL.B.

EXPERIMENTAL PSYCHOLOGY. A Series of Broadcast Talks. Edited by B. A. Farrell. Philosophical Library, New York. Pp. 66. $2.75.

This is a short treatise, the report of a series of talks broadcast over BBC. The experts who gave the reports are A. J. Watson, Harry Kay, J. A. Deutsch, B. A. Farrell, Michael Argyle, and R. C. Oldfield. All are experimental psychologists and all are interested in some particular phase of the subject.

These talks were given in an effort to clarify for the public the contributions of the experimental psychologists because, as the editor notes, their work has been surrounded by various misconceptions, dogged by poor public relations, and its importance apt to be missed "between the more striking work of the psychiatrists and psychoanalysts on one hand and the physiologists and neurologists on the other."

There are six chapters encompassing: 1. Perception; 2. Adult Learning and Remembering; 3. Motivation; 4. Some Hypotheses of Psychoanalysis; 5. The Study of Social Behavior; and the last, The Prospects of Experimental Psychology, which assays the possibilities of this discipline in the future.

The report is interesting; it clarifies for the layman some of the problems which interest the experimentalist; and it accentuates his importance in the scheme of things.

Francis J. Braceland, M.D.

THE NEUROSES IN CLINICAL PRACTICE. By Henry P. Laughlin, M.D., Assistant Clinical Professor of Psychiatry, George Washington University School of Medicine; Head, Psychiatry, Walter Reed Army Medical Center. Cloth. $12.50. Pp. 802, with 216 illustrative case summaries. W. B. Saunders Company, Philadelphia, 1956.

The author is to be highly commended for his presentation of a comprehensive textbook and a reference source for those seeking knowledge in this field. In fourteen chapters he presents a wealth of material answering a long felt need for a book of this scope and practicality on the neuroses. He has used the term neuroses to include psychoneuroses, character neuroses, depressions, traumatic neuroses and fatigue reactions thereby widening the area of discussion.

The contents are well organized and very current. Ataractic drug therapy, for instance is included and given a proper place in the over-all therapeutic perspective. He writes very lucidly and his basic English proves to be easily read. He has discussed emotional disorders which are frequently encountered in clinical practice and given them emphasis in accordance with this. His presentation is a dynamically oriented one with stress laid on the psychodynamics and pathogenesis of neurotic reactions. Included with the descriptions of these reactions are over two hundred case summaries to illustrate different concepts as well as the disorders themselves. There are also over thirty tables provided which well summarize and graphically illustrate points made throughout the text.

The opening chapter on anxiety provides an introduction, stressing the relativity of emotional health, as well as a discussion on the nature, origin and function of anxiety. The succeeding chapter

on anxiety reactions is concerned with acute and chronic anxiety reactions and anxiety neurosis. The pattern in this chapter of presenting the historical background, diagnosis, symptoms, psychodynamics and treatment is followed throughout the text as he discusses each reaction pattern. The therapeutic approach is a very practical one without stress on the cliches which are so frequently seen elsewhere. The importance of diagnosis on a positive basis rather than by exclusion of organic illness is emphasized.

Chapter three on the mental mechanisms is the longest in the book. It is well written and clearly relates these concepts to the neuroses through many case illustrations. The clarity of the presentation of this aspect of basic psychiatry is one of the high points in the author's presentation. The next two chapters are concerned with phobic reactions, with fear and its avoidance covered in one and the phobias in the other. The author has coined the term soteria which he defines as "the converse of a phobia" and which he discusses in this chapter as well as including it in his classification of the neuroses.

Chapter six covers the primary gain (endogain) and secondary gain (epigain) of emotional illness. There are discussions of the conversion reactions and dissociative reactions in the following chapter. As applicable the character defenses associated with these neurotic reactions are included in the discussions about them. Extensive references are provided following the summary of each chapter.

Depressions of neurotic and psychotic magnitude as well as the depressive character defenses are presented in chapter nine. Tables relative to th clinical and personal experience of physicians and students with suicidal tendencies point out the frequency of morbid depressions. The reviewer differs with the author in his relative de-emphasis of the use of electroshock therapy in depressions and would stress the frequent practical need of this therapy as opposed to the lesser availability of intensive psychotherapy. The pros and cons of such therapy are discussed by the author, however.

The fatigue reactions and overconcern with health including hypochondriasis and somatic and/or physiologic preoccupation are the titles of chapters ten and eleven. The obsessive-compulsive reactions in the succeeding two chapters including the obsessive-compulsive neurosis, obsessive character defenses, obsessive personality and the obsessive type of character neurosis are presented in considerable detail. The concluding chapter is on the neuroses following trauma. The author's estimate of the clinical incidence of neurotic reactions as presented in a table is of considerable interest.

He has prepared a brief nomenclature of emotional and mental illness including the psychologically determined neurotic reactions as presented in the text as well as other illnesses beyond the scope of this volume. Fifteen hundred psychiatric concepts and terms are briefly defined in a glossary and provide a very valuable reference source. This should prove particularly valuable to the medical student. An index of personal names and a vast fifty-three page index of subjects concludes the book.

This book should become a standard psychiatric textbook. It will very well serve this function for the medical student. It is of great value as a standard volume in the library of the psychiatrist and is a recommended reference source for other physicians and those in allied fields seeking knowledge about the neuroses.

Leigh M. Roberts, M.D.

BOOKS RECEIVED

NEUROLOGY AND PSYCHIATRY IN CHILDHOOD: By Rustin McIntosh, M.D., and Clarence C. Hare, M.D., Editors. Cloth. $11.00. Pp. 504. Williams & Wilkins Company, Baltimore, Maryland, 1954.

YEAR BOOK OF NEUROLOGY PSYCHIATRY AND NEUROSURGERY: Edited by Roland P. Mackay, M.D., et al. Cloth. $7.00. Pp. 576. Year Book Publishers, Inc., 200 E. Illinois St., Chicago, Ill., 1956.

CARDIOVASCULAR INNERVATION: By G. A. GG. Mitchell, O.B.E., T.D., M.B., ChM., D. Sc. Professor of Anatomy and Director of the Anatomical Lab. in the University of Manchester. Cloth. $11.00. Pp. 356. The Williams & Wilkins Co., Baltimore 2, Maryland, 1956.

RECENT ADVANCES IN NEUROLOGY AND NEUROPSYCHIATRY: By Sir Russell Brain, Bt. D.M. (Oxon) P.R.C.P., Physician to the London Hospital and the Maida VVale Hospital for Nervous Diseases, and E. B. Strauss, M.A., D.M. (Oxon) D. Sc., F.R.C.P., Physician for Psychological Medicine, St. Bartholomew's Hospital. Cloth. $7.50. Pp. 311. Little, Brown & Company, 34 Beacon Street, Boston, Mass., 1955.

HEALTH OBSERVATION OF SCHOOL CHILDREN: By George M. Wheatley, M.D., M.P.H. and Grace T. Hallock. Cloth. $6.50. Pp. 488. McGraw-Hill Book Company, Inc., 330 W. 42nd Street, New York 36, N. Y. Second Edition, 1956.

CURRENT THERAPY: Edited by Howard F. Conn, M.D., and other Consulting Editors. Cloth. $11.00. Pp. 632. W. B. Saunders Company, West Washington Square, Philadelphia, Penna. 1956.

IMPARTIAL MEDICAL TESTIMONY: A report by a Special Committee of the Association of the Bar of the City of New York, Cloth. $3.95. Pp. 188. The Macmillan Company, 60 Fifth Avenue, N. Y. 1956.

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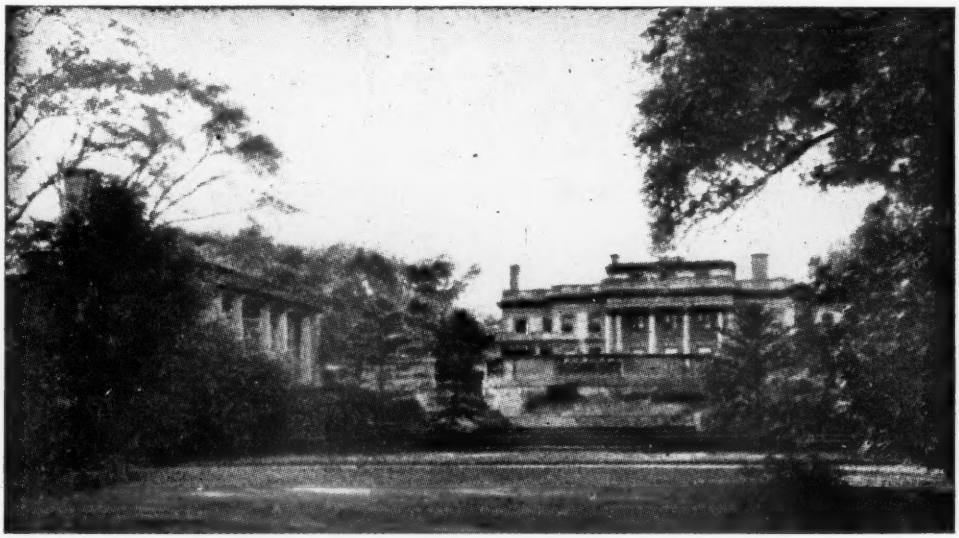

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